CRISPR Therapeutics Announces Preclinical Data at the American Heart Association (AHA) Scientific Sessions 2023

-CTX310™ led to durable reductions of angiopoietin-like 3protein (ANGPTL3) and triglyceride levels in non-human primates (NHPs) after a single dose-

-CTX320™ led to durable reductions of lipoprotein(a) (Lp(a)) levels in NHPs after a single dose-

-Both CTX310™ and CTX320™ were well-tolerated in NHPs at clinically relevant dose levels-

-Clinical trial initiated for CTX310™, targeting ANGPTL3-

-CTX320™ targeting Lp(a) is on track to enter the clinic in the first half of 2024-

ZUG, Switzerland and BOSTON, Nov. 06, 2023 (GLOBE NEWSWIRE) -- CRISPR Therapeutics (Nasdaq: CRSP), a biopharmaceutical company focused on creating transformative gene-based medicines for serious diseases, today announced preclinical data from the Company's investigational programs for the treatment of cardiovascular disease, at the American Heart Association (AHA) Scientific Sessions 2023. The data will be presented on Saturday, November 11, 2023, in two oral sessions, entitled "CTX310: An Investigational *in vivo* CRISPR-Based Therapy Efficiently and Durably Reduces ANGPTL3 Protein and Triglyceride Levels in Non-Human Primates After a Single Dose" and "CTX320: An Investigational *in vivo* CRISPR-Based Therapy Efficiently and Durably Reduces Lipoprotein(a) Levels in Non-Human Primates After a Single Dose."

"We're excited to share these preclinical data at AHA highlighting the progress made across our *in vivo* programs targeting ANGPTL3 and Lp(a). The findings demonstrate the potential of a one-time treatment to produce clinically meaningful, long-lasting reductions in risk factors for atherosclerotic cardiovascular disease," said Phuong Khanh (P.K.) Morrow, M.D., FACP, Chief Medical Officer at CRISPR Therapeutics. "These data increase our confidence in our goal to shift the treatment paradigm for patients at risk of cardiovascular disease away from burdensome chronic care to a potentially one-time, durable therapy."

CRISPR Therapeutics is advancing a pipeline of *in vivo* gene editing programs using lipid nanoparticle (LNP) delivery of Cas9 mRNA and a guide RNA (gRNA) to the liver. The first two *in vivo* programs, CTX310 and CTX320, each aim to reduce expression of a validated target for cardiovascular disease.

CTX310 is an investigational *in vivo* CRISPR/Cas9 gene editing therapy designed to knock out hepatic expression of angiopoietin-like 3 protein (ANGPTL3). In humans, naturally occurring loss-of-function variants in *ANGPTL3* are associated with reduced levels of serum lipids and reduced risk of atherosclerotic cardiovascular disease. In the preclinical data to be presented at AHA, treatment of non-human primates (NHPs) with a single dose of CTX310 led to mean editing of *ANGPTL3* in the liver of 70%, and corresponding mean reductions in plasma ANGPTL3 protein of more than 85% and triglycerides of 60%. Reductions in ANGPTL3 protein and triglycerides were durable past a year post-treatment. CTX310 was well-tolerated in NHPs with only transient elevation of liver enzymes that resolved without intervention. These data suggest that CTX310 has the potential to be used to treat dyslipidemias in humans.

CTX320 is an investigational *in vivo* CRISPR/Cas9 gene editing therapy to reduce hepatic expression of lipoprotein(a) (Lp(a)). Genetic and epidemiological studies in humans have identified elevated levels of Lp(a) as an independent risk factor of atherosclerosis and related diseases. In the preclinical data to be presented at AHA, treatment of NHPs with a single dose of CTX320 led to a mean reduction in plasma Lp(a) of 95%. This reduction was durable past a year post-treatment. CTX320 had a well-tolerated safety profile similar to that of CTX310. These data suggest CTX320 has the potential to be used to reduce plasma Lp(a) levels in humans.

About CRISPR Therapeutics

CRISPR Therapeutics is a leading gene editing company focused on developing transformative gene-based medicines for serious diseases using its proprietary CRISPR/Cas9 platform. CRISPR/Cas9 is a revolutionary gene editing technology that allows for precise, directed changes to genomic DNA. CRISPR Therapeutics has established a portfolio of therapeutic programs across a broad range of disease areas including hemoglobinopathies, oncology, regenerative medicine and cardiometabolic diseases. To accelerate and expand its efforts, CRISPR Therapeutics has established strategic partnerships with leading companies including Bayer, Vertex Pharmaceuticals and ViaCyte, Inc. CRISPR Therapeutics AG is headquartered in Zug, Switzerland, with its

wholly-owned U.S. subsidiary, CRISPR Therapeutics, Inc., and R&D operations based in Boston, Massachusetts and San Francisco, California, and business offices in London, United Kingdom. For more information, please visit www.crisprtx.com.

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CRISPR Therapeutics Forward-Looking Statement

This press release may contain a number of "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements made by Dr. Morrow in this press release, as well as statements regarding CRISPR Therapeutics' expectations about any or all of the following: (i) the safety, efficacy and progress of CRISPR Therapeutics' various clinical and preclinical programs; (ii) the status of clinical trials and preclinical studies (including, without limitation, expectations regarding the oral presentations, the data that is being presented, and the expected timing of data releases and initiation of clinical trials); and (iii) the therapeutic value, development, and commercial potential of CRISPR/Cas9 gene editing technologies and therapies. Without limiting the foregoing, the words "believes," "anticipates," "plans," "expects" and similar expressions are intended to identify forward-looking statements. You are cautioned that forward-looking statements are inherently uncertain. Although CRISPR Therapeutics believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: uncertainties inherent in the initiation and completion of preclinical studies for its product candidates and whether results from such studies will be predictive of future results of future studies or clinical trials; the potential that clinical trial results may not be favorable or may not support registration or further development; that one or more of its clinical and preclinical programs will not proceed as planned for technical, scientific or commercial reasons; the potential that future competitive or other market factors may adversely affect the commercial potential for CRISPR Therapeutics' product candidates; uncertainties regarding the intellectual property protection for CRISPR Therapeutics' technology and intellectual property belonging to third parties; and those risks and uncertainties described under the heading "Risk Factors" in CRISPR Therapeutics' most recent annual report on Form 10-K , quarterly report on Form 10-Q and in any other subsequent filings made by CRISPR Therapeutics with the U.S. Securities and Exchange Commission, which are available on the SEC's website at www.sec.gov. CRISPR Therapeutics disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this press release, other than to the extent required by law.

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